Estimating the Burden of Disease and the Benefits of Prevention

Patricia Hartge

Of the 2.4 million U.S residents who died in 2000, some died prematurely. A portion of these excess deaths were due to obesity, presumably reflecting the effects of poor diet or physical inactivity. According to Mokdad et al,[1,2] there were 365,000 deaths attributable to this complex of causes in 2000. This estimate came by applying the summarized hazard ratios from 6 cohort studies to population survey data. Not long thereafter, Flegal et al[3] estimated that obesity had produced only 112,000 excess deaths based on NHANES survey and follow-up data. Does obesity account for one in 7 U.S. deaths, one in 20, or some other fraction?

In this issue, Steenland and Armstrong[4] discuss methods for estimating the burden of disease as imposed by a particular cause. The same methodologic concerns underlie other computations of possible health gains, for example, the numbers of women who would benefit from taking tamoxifen.[5] Steenland and Armstrong suggest some ways in which we can express health burdens with more sophistication using a wider range of metrics to capture years of life lost or diminished. (The authors do not recommend venturing further into dollars spent or earnings foregone, apparently taking that as the boundary between epidemiology and economics.)

For interested researchers, there is a rich and growing literature on comparing burdens of disease. For example, Brown et al[6] illustrate how the diverse measures of cost, occurrence (incidence, prevalence, and mortality), and health-related quality of life each shed a different light on comparisons among cancers. This expanded set of indicators also can be applied to specific exposure–disease pairs. If obesity-related deaths occur later in life and tobacco-related ones earlier, for example, public health strategies may need to be tailored accordingly.

Some epidemiologists will prefer to concentrate on measuring effects, leaving the downstream estimation and evaluation of long-term costs and benefits to others. Steenland and Armstrong implicitly argue that epidemiologists should be the ones to trace the broader impact of an exposure if only because epidemiologists are the ones who best understand the estimates of biologic effects and rates of disease occurrence that determine long-term impact. It makes sense that epidemiologists, as public health practitioners, should consider wider frames of reference.

If there is one measure of impact that epidemiologists are most likely to report, it is the attributable proportion (or attributable fraction), the main topic of Steenland and Armstrong's essay. Motivated in part by the literature on occupational risk and on the effects of closely related behaviors such as smoking and drinking, the authors offer sound advice on handling recognized confounders, known interactions, and exposure gradients. They warn of the typical traps in calculating the attributable proportion, including several of the egregious errors noted by Rockhill et al.[7]

Steenland and Armstrong devote considerable attention to precision and suggest suitable variance calculations. Capturing imprecision surely matters, but avoiding bias matters more. "Portability" is their general term for the legitimacy of applying the results of one or more studies to the population at large. The authors see this as analogous to

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external validity, but this limited construction tends to obscure the larger fact that portability lies at the heart of most disputes on the true burden of disease.

The wide variation in the previously mentioned estimates of obesity-related deaths is more a problem of uncertain validity of the reported risks than of random variation. This is typical of most estimates of attributable risk associated with behaviors or environmental exposures. (In exceptional circumstances, one can measure the rates of disease in the relevant exposure groups of the total population; then the absolute rates directly yield both burden and effect measures.) Along the same lines, all would agree that an association should be causal for an estimate of attributable proportion or fraction to make sense. However, of course, we need more than that; we need an accurate estimate of the magnitude of the effect (be it relative risk or risk difference) and an accurate estimate of the fraction of cases or controls exposed. A particular study may provide an accurate estimate of one component but an inaccurate estimate of another.

In the obesity-mortality example, the uncertainty stems largely from errors in the relative risks (RRs). Respectable studies with different designs often give a range of results, probably less from random variation than from competing systematic biases. Smoking confounds the association because it reduces weight and increases risk of death; analysts handle the problem differently in different estimates. Physical activity alters weight but also alters mortality risk at any particular weight. Recent weight loss may presage illness leading to death. The magnitudes of relative risks along the classic U-shape play a critical role with the point of lowest mortality at somewhat different body mass levels in different studies with different exclusions and adjustments and different sources of data on height and weight. Because many people in the United States have weights near the uncertain upward slope of the U, discrepancies in RR estimates that would barely alter what we infer about the biology of adiposity and health nonetheless can change the apparent disease burden.

For situations in which we think we know the relative risk, Steenland and Armstrong challenge us to rethink our views on what should be the next step. For some purposes, the total population burden may be salient, whereas for other purposes, we may want to know a series of absolute risks (for example, across particular body mass indices). Oddly enough, a range of absolute risks might be less controversial than a computation of total burden and more likely to provide clear public health guidance.

Should epidemiologists "use these measures [of disease burden] more frequently when presenting results," as Steenland and Armstrong advise? Accurate calculations of disease burden can impose different, and sometimes stronger, requirements than accurate estimation of RR, as the obesity-mortality story illustrates. Relative risk is a sturdy measure that captures a common biologic effect as it occurs across a range of settings and study bases. Often, an individual epidemiologic study succeeds in producing a roughly valid estimate of RR, and yet it may not be suitable to estimate disease burden in any population beyond the study members. In that situation, publication of burden estimates may only muddy the waters. As the accumulation of data provides us with increased confidence in the validity of our risk estimates and also the frequencies of exposure, we can proceed with greater confidence to estimate disease burden and the options for prevention.

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